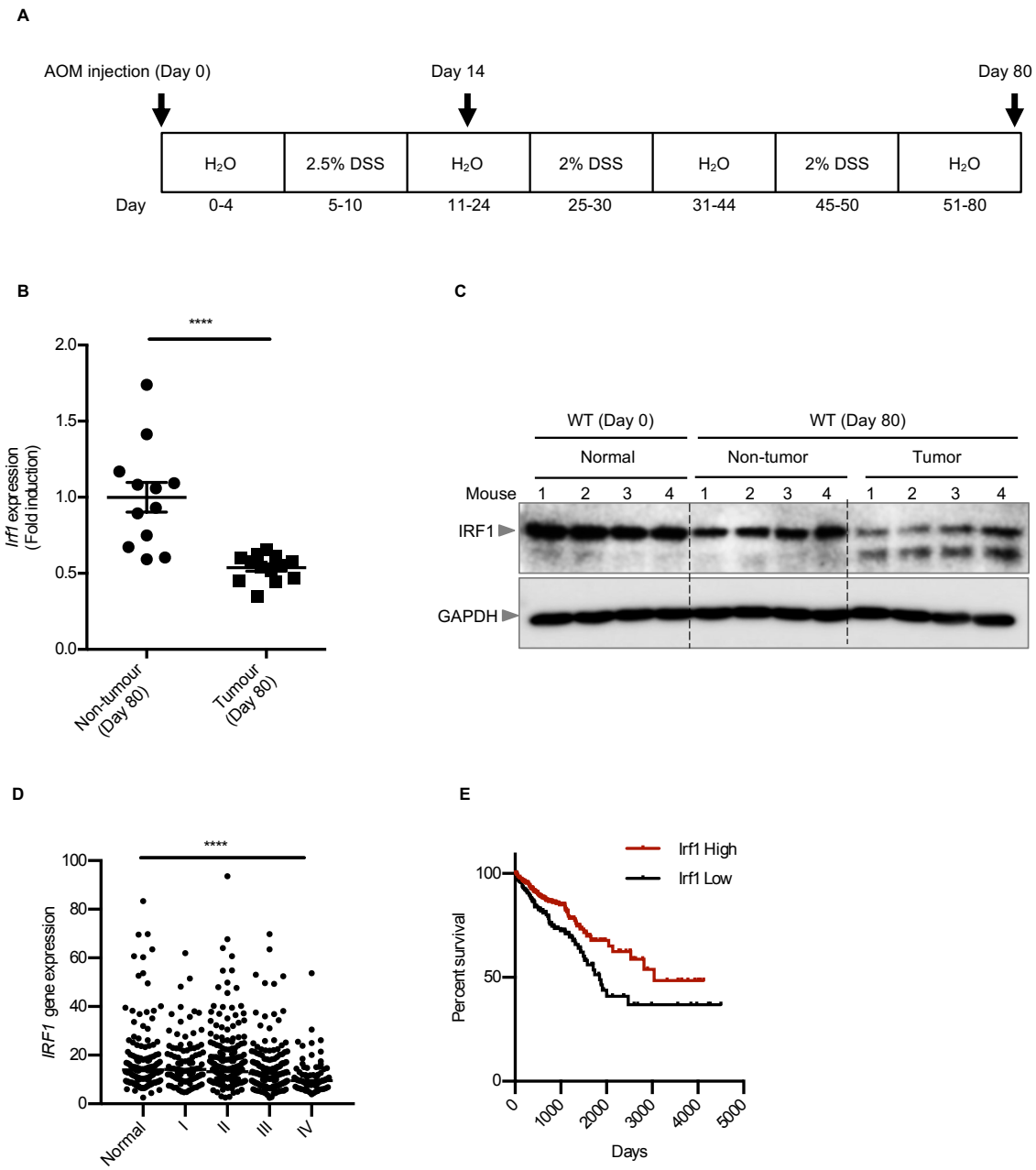
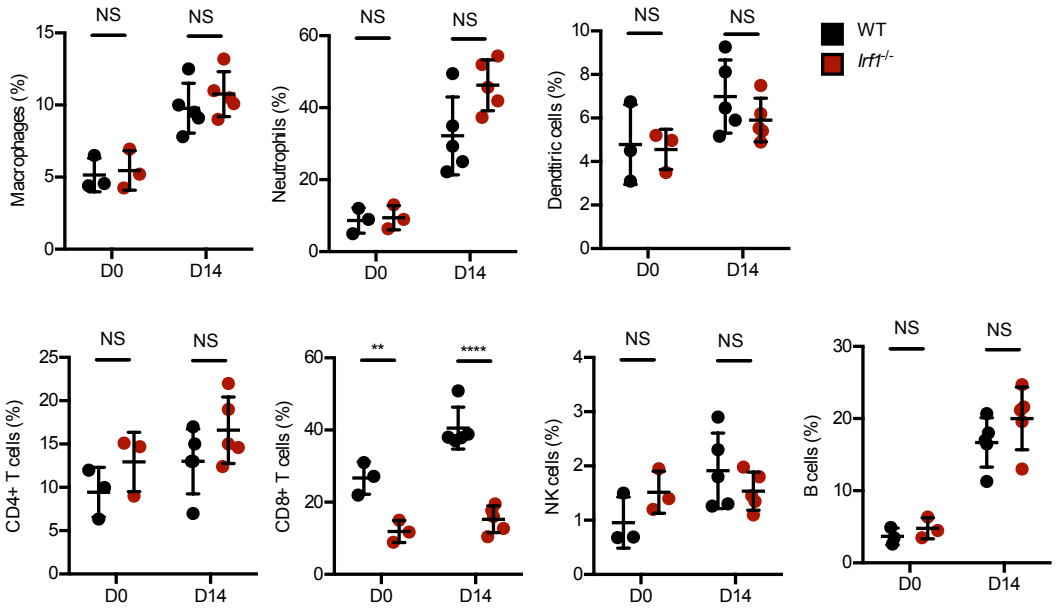


Supplementary Figure 1. The expression of IRF1 in tumor and non-tumor colon samples

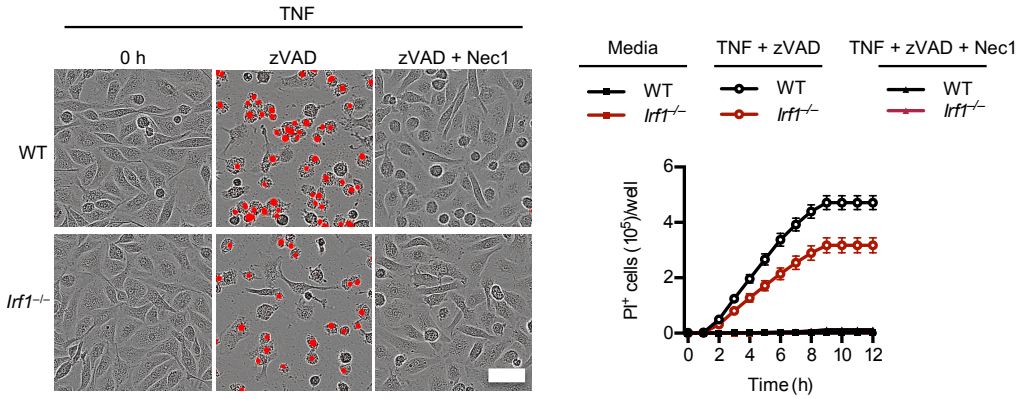
(A) Timeline for azoxymethane (AOM) and dextran sulfate sodium (DSS) treatment in mice. (B) Relative expression of the gene encoding IRF1 in non-tumor and tumor tissue in the colons of wild type (34) mice 80 days after AOM injection. (C) Immunoblot analysis of IRF1 in the colons of WT mice on day 0 and in tumor and non-tumor tissue on day 80 after AOM injection. Blots represent data from the same biological samples run in parallel. (D) Analysis of data from the

TCGA database for *IRF1* mRNA expression in human CRC samples obtained at different stages of the disease. (E) Kaplan-Meier survival curve of patients with colorectal cancer with high or low *IRF1* gene expression. Patients were classified into either high or low *IRF1* expression using the best expression cutoff criterion described in the Human Protein Atlas (58, 59). Each symbol represents an individual mouse in B and an individual clinical isolate in D. Data are from one experiment representative of three independent experiments in B and C. ****$P < 0.0001$. The two-tailed t-test (B), one-way ANOVA (D), and log-rank (Mantel-Cox) test (E) were used. Data are represented as mean ± SEM in B and D.



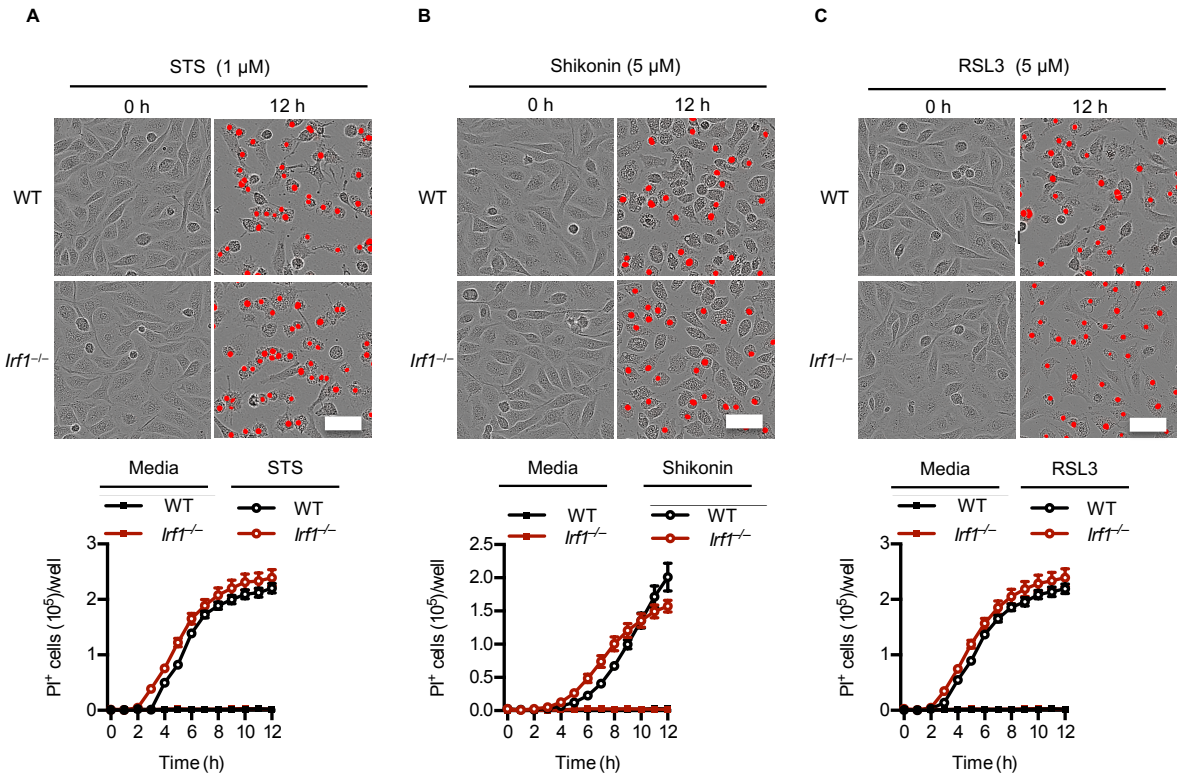
Supplementary Figure 2. Role of IRF1 in infiltrating immune cells during colitis

The percentages of macrophages, neutrophils, dendritic cells, NK cells, $CD8^+$ T cells, and $CD4^+$ T cells per colon in WT and *Irf1*$^{-/-}$ mice 14 days after injection of azoxymethane (AOM). ***P* < 0.01 *****P* < 0.0001; NS, not statistically significant. The two-way ANOVA was used. Data are represented as mean ± SEM.



Supplementary Figure 3. IRF1 promotes necroptosis.

Real-time cell death analysis by IncuCyte and propidium iodide (PI) staining in bone marrow-derived macrophages (BMDMs) after stimulation with TNF, TNF + zVAD, or TNF + zVAD + Nec1 (TNF 50 ng/mL; zVAD 25 μM; Nec1 25 μM) for 0 or 6 h. Scale bar, 500 μM. Data are from one experiment representative of two independent experiments. Data are represented as mean ± SEM.



Supplementary Figure 4. IRF1 is dispensable for cell death in response to classical cell death inducers.

(A–C) Real-time cell death analysis by IncuCyte and propidium iodide (PI) staining in bone marrow-derived macrophages (BMDMs) after stimulation with staurosporine (STS; 1 μM) for 12 h (A), shikonin (5 μM) for 12 h (B), or RSL3 (5 μM) for 12 h (C). Scale bar, 500 μM. Data are from one experiment representative of two independent experiments. Data are represented as mean ± SEM.

SUPPLEMENTARY TABLE

Supplementary Table 1. Real-time qPCR primer sequences

Target	Primer sequence
m*Irf1*	Forward: 5'-GTG AAC TAC TGG GCT TTC-3'
	Reverse: 5'-CTG GGA TTT GGT TGG AAT T-3'
m*Hprt*	Forward: 5'-CTC ATG GAC TGA TTA TGG ACA GGA C-3'
	Reverse: 5'-GCA GGT CAG CAA AGA ACT TAT AGC C-3'